K 111335

Tosoh Bioscience, Inc.

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510(k) Summary

ST AIA-PACK ACTH

Date:	**August 16, 2011**
Submitter:	**Tosoh Bioscience, Inc** **3600 Gantz Road** **Grove City, OH 43123**
Contact Person:	**Judith K. Ogden** **Director, New Business & Technical Development** **6000 Shoreline Ct., Ste. 101** **South San Francisco, CA 94080** **Phone: 650-636-8112** **Fax: 650-636-8113** **Email: Judy.Ogden@tosoh.com**
Device Name:	**ST AIA-PACK ACTH**
Classification:	**Class II** **CKG** **Clinical Chemistry** **21 CFR 862.1025**
Device Name:	**ST AIA-PACK ACTH Calibrator Set**
Classification	**Class II** **JIT** **Clinical Chemistry** **21 CFR 862.1150**
Device Name:	**AIA-PACK ACTH Control Set**
Classification	**Class I** **JJX** **Clinical Chemistry** **21 CFR 862.1660**
Predicate Device:	**k 060585** **Roche Diagnostics** **Elecsys ACTH Immunoassay** **Elecsys ACTH CalSet**

510(k) Summary

ST AIA-PACK ACTH

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Device Description:

The ST AIA-PACK ACTH is a two-site immunoenzymometric assay which is performed entirely in the ST AIA-PACK ACTH test cups. ACTH present in the test sample is bound with anti-ACTH goat polyclonal antibody immobilized on magnetic beads and enzyme-labeled anti-ACTH goat polyclonal antibody. The magnetic beads are washed to remove unbound enzyme-labeled anti-ACTH goat polyclonal antibody and are then incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The enzyme alkaline phosphatase causes oxidation of 4MUP to 4MU. 4MU is excited at 365 nm and comes to ground state at 448 nm releasing florescent energy. The amount of florescent energy is measured by the detector.

The amount of enzyme-labeled anti-ACTH goat polyclonal antibody that binds to the beads is directly proportional to the ACTH concentration in the test sample. A standard curve is constructed, and unknown sample concentrations are calculated using this curve.

The following products are required to use the ST AIA-PACK ACTH	P/N 025221:
ST AIA-PACK ACTH Calibrator Set	P/N 025321
ST AIA-PACK ACTH Sample Diluting Solution	P/N 025521
AIA-PACK ACTH Control Set	P/N 025421

Device Intended Use:

ST AIA-PACK ACTH is designed for IN VITRO DIAGNOSTIC USE ONLY for the quantitative measurement of adrenocorticotropic hormone (ACTH) in human EDTA plasma. Measurements of ACTH are useful in the differential diagnosis and treatment of certain disorders of the adrenal glands such as Cushing's syndrome, adrenocortical insufficiency, and the ectopic ACTH syndrome.

ST AIA-PACK ACTH Calibrator Set is intended for IN VITRO DIAGNOSTIC USE ONLY for the calibration of the ST AIA-PACK ACTH assay on Tosoh AIA Systems Analyzers.

The AIA-PACK ACTH Control Set is intended for IN VITRO DIAGNOSTIC USE ONLY for performing quality control procedures with the ST AIA-PACK ACTH Assay.

Substantial Equivalence:

Comparison between the Tosoh ST AIA-PACK ACTH and the Roche Diagnostics Elecsys ACTH Immunoassay

Similarities:

Item	Device	Predicate
	ST AIA-PACK ACTH	**Elecsys ACTH**
Intended Use	ST AIA-PACK ACTH is designed for IN VITRO DIAGNOSTIC USE ONLY for the quantitative measurement of Adrenocorticotropic hormone (ACTH) in human EDTA plasma on Tosoh AIA System Analyzers.	Immunoassay for the in vitro quantitative determination of adrenocorticotropic hormone (ACTH) in human EDTA plasma. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.
Intended Use Calibrators	ST AIA-PACK ACTH Calibrator Set is intended for IN VITRO DIAGNOSTIC USE ONLY for the calibration of the ST AIA-PACK ACTH assay on Tosoh AIA Systems Analyzers.	Elecsys ACTH CalSet is used for calibrating the quantitative Elecsys ACTH assay on the Elecsys immunoassay analyzers.
Intended Use Controls	The AIA-PACK ACTH CONTROL SET is intended for IN VITRO DIAGNOSTIC USE ONLY for performing quality control procedures with the ST AIA-PACK ACTH Assay.	Elecsys PreciControl ACTH is used for quality control of the Elecsys ACTH immunoassay on the Elecsys immunoassay analyzers.
Indications for Use	Plasma ACTH measurements are useful in the differential diagnosis of pituitary Cushing's disease (ACTH hypersecretion), adrenocortical insufficiency (Addisons disease), pituitary tumors (e.g. Nelson's syndrome), hypopituitarism with ACTH deficiency and ectopic ACTH syndrome.	ACTH measurements are used in the differential diagnosis and treatment of certain disorders of the adrenal glands such as Cushings syndrome, adrenocortical insufficiency, and ectopic ACTH syndrome.
Assay Protocol	Sandwich assay	Sandwich Assay
Sample Type	Human EDTA Plasma	Human EDTA Plasma
Assay Low	2.0 pg/mL	1.0 pg/mL

Assay High	2000 pg/mL	2000 pg/mL
Reference Range	7.4-64.3 pg/mL	7.2-63.3 pg/mL
Hook Effect	No high dose hook effect up to 1,000,000 pg/mL	No high dose hook effect up to 1,000,000 pg/mL
Control level	Two levels of control; lyophilized	Two levels of control; lyophilized

Differences:

Item	**Device**	**Predicate**
	ST AIA-PACK ACTH	**Elecsys ACTH**
Detection Protocol	Fluorescence	Electrochemiluminescent
Calibrator	ST AIA-PACK Calibrator Set 6-Point	ACTH CalSet 2-Point
Calibration Interval	90 days when using same test cup lot	3-28 Days depending on analyzer and storage conditions
Calibration Verification	6-Point Calibration does not require calibration verification material	3 levels ACTH CalCheck
Traceability / Standardization	ACTH (Human, 1-39) Bachem AG: code. H-1160; gravimetric preparation	Standardized gravimetrically with synthetic ACTH produced by Roche
Base Matrix (Control & Calibrator)	MOPSO Buffer with 5% Bovine Serum Albumin	Equine serum
Reconstituted stability	Up to 7 days when stored at 2 - 8° C when not in use.	Up to 3 hours at 20 - 25° C; - 20° C one month.

Precision:

The precision study was developed with reference to the CLSI protocol entitled: Evaluation of Precision Performance of Quantitative Measurement Methods (EP5-A2).

The precision study for the ST AIA-PACK ACTH assay was evaluated utilizing three AIA-2000 analyzers and 3 different lots of reagents. Precision was assessed by assaying three levels of unaltered EDTA plasma specimens. Estimates of total and within-run precision were obtained from measurements of 2 replicates in a single run, 2 times a day for 20 non-consecutive days. This equaled to a total of 40 runs and 80 determinants.

Within Run Precision:

Specimen	Reagent Set # 1			Reagent Set # 2			Reagent Set # 3		
	Mean (pg/mL)	Pooled SD	CV %	Mean (pg/mL)	Pooled SD	CV %	Mean (pg/mL)	Pooled SD	CV %
EDTA Plasma-A	37.8	1.2	3.1	44.3	1.2	2.8	40.9	0.89	2.2
EDTA Plasma-B	223.7	4.8	2.1	244.6	5.1	2.1	230.0	5.3	2.3
EDTA Plasma-C	709.2	10.9	1.5	740.4	15.6	2.1	719.1	15.5	2.2

Total Precision:

Specimen	Reagent Set # 1			Reagent Set # 2			Reagent Set # 3		
	Mean (pg/mL)	Pooled SD	CV %	Mean (pg/mL)	Pooled SD	CV %	Mean (pg/mL)	Pooled SD	CV %
EDTA Plasma-A	37.8	1.2	3.3	44.3	1.9	4.2	40.9	1.03	2.5
EDTA Plasma-B	223.7	5.7	2.5	244.6	9.3	3.8	230.0	6.4	2.8
EDTA Plasma-C	709.2	15.6	2.2	740.4	25.1	3.4	719.1	15.9	2.2

Linearity:

The linearity study was developed with reference to the CLSI protocol entitled: Evaluation of the Linearity of Quantitative Measurement Procedures (EP6-A).

The repeatability CV% met the criterion of </= 10%. Therefore, the ST AIA-PACK ACTH has been demonstrated to be linear from 2.0 to 2,000 pg/mL.

Correlation:

The methods comparison study was conducted with reference to the CLSI protocol entitled: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP9-A2).

A total of 160 EDTA plasma specimens (154 unaltered and 6 altered specimens) were assayed in singleton utilizing the ST AIA-PACK ACTH assay on the AIA-2000 analyzer and the Roche Elecsys-ACTH on the MODULAR ANALYTICS E170 (Elecsys module) analyzer. A combination of fresh and frozen specimens was utilized for this study. Six of the 160 specimens were mixed using two or more specimens and altered.

Regression Analysis		
	Deming	**Regular**
Slope:	1.10 (1.075 to 1.116)	1.09 (1.067 to 1.107)
Intercept:	-0.84 (-8.921 to 7.234)	0.76 (-7.305 to 8.817)
95% Confidence Intervals are shown in parentheses		
Corr Coef (R):	0.993	
Bias: (all samples)	17.8 pg/mL	
Points (Plotted/Total):	160/160	
Result Ranges:	3.8 to 1986 pg/mL	

The mean bias at the medical decision point (between 7.4 and 64.3 pg/mL) is 4.87 pg/mL. The bias at 7.73 pg/mL is -0.87 pg/mL. The bias at 64.97 pg/mL is -17.93 pg/mL.

Limit of Detection (LoD) and Limit of Quantitation (LoQ):

The LoB and LoD for ST AIA-PACK ACTH was determination was based on guidance from CLSI Protocol EP17-A. While the calculated LoQ is 1.2 pg/mL, the assay low claim is 2.0 pg/mL. This value is a conservative claim in the event of lot-to-lot variability.

The LoB was determined to be 0.5 pg/mL.
The LoD was determined to be 0.7 pg/mL.
The LoQ was determined to be 1.2 pg/mL

Interference:

The criterion for recovery was set at 100 +/- 10%. If a specimen recovered within 100 +/- 10%, it was considered as no interference from the particular substance.

1. Added hemoglobin (up to 440 mg/dL) did not interfere with the assay.
2. Conjugated bilirubin (up to 19 mg/dL) and free bilirubin (up to 17 mg/dL) did not interfere with the assay.
3. Lipemia, as indicated by added triglyceride (up to 1,600 mg/dL), did not interfere
4. Ascorbic acid (up to 20 mg/dL) did not interfere with the assay.
5. EDTA•2K (up to 7 mg/mL) did not interfere with the assay.
6. Protein, as indicated by human albumin concentrations (up to 5.0 g/dL), did not interfere with the assay.
7. Rheumatoid factor did not interfere with ACTH assay up to 500 IU/mL.
8. Heparin (up to 50 U/mL) does not interfere with the assay.
9. Acetominaphen (up to 20 mg/L) does not interfere with the assay.
10. Acetylsalicylic acid (up to 300 mg/L) does not interfere with the assay.
11. Ampicillin (up to 200 mg/L) does not interfere with the assay.
12. Ibuprofen (up to 50 mg/L) does not interfere with the assay.
13. Theophylline (up to 10 mg/L) does not interfere with the assay.

Specificity:

The recovery of ACTH should be within 90 - 110%.

ACTH Fragment	ACTH fragment conc. [pg/mL]	Measured ACTH conc. [pg/mL]			Difference (measured – original)	ACTH Recovery [%]	% Cross-reactivity
		Value -1	Value -2	Average			
(Control)	0	55.1	53.6	54.3	---	---	---
ACTH 1-10	500	54.4	54.2	54.3	0.0	100%	-0.01%
	5,000	55.0	54.4	54.7	0.4	101%	0.01%
	100,000	55.3	56.1	55.7	1.3	102%	0.00%
ACTH 11-24	500	53.5	53.4	53.4	-0.9	98%	-0.18%
	5,000	54.1	53.0	53.6	-0.8	99%	-0.02%
	100,000	53.8	53.8	53.8	-0.5	99%	0.00%
Beta-MSH	500	53.7	54.0	53.8	-0.5	99%	-0.10%
	5,000	54.1	54.9	54.5	0.2	100%	0.00%
	100,000	51.1	52.1	51.6	-2.8	95%	0.00%
Beta-Endorphin	500	53.1	53.0	53.0	-1.3	98%	-0.26%
	5,000	54.9	53.5	54.2	-0.1	100%	0.00%
	100,000	53.1	52.5	52.8	-1.5	97%	0.00%

ACTH 1-10, 11-24, beta-MSH and beta-Endorphin do not interfere the assay up to 100,000 pg/mL.

ACTH recovery was less than 90% in the presence of ACTH 1-17, 1-24, 18-39, alpha-MSH (>5,000pg/mL) or ACTH 22-39 (>100,000 pg/mL). These fragments may negatively affect the ACTH assay. It is likely that these fragments bind to either the antibodies on beads or the enzyme-labeled antibodies. Therefore, if these fragments were contained excessively in the test sample, lower values may be reported.

Standards:

Number	FDA Recognition Number	Revision Date	Title
C28-A3	7-202	09/08/2009	How to Define and Determine Reference Intervals in the Clinical Laboratory-Third Edition
EP5-A2	7-110	10/31/2005	Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline- Second Edition
EP6-A	7-193	03/18/2009	Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline
EP9-A2	7-92	03/08/2004	Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition
EP17-A	7-194	03/18/2009	Protocols for Determination of Limits of Detection and Limits of Quantitation: Approved Guideline

Control Value Assignment:

The control value assignments are established on 2 analyzers with 2 lots of ST AIA-PACK ACTH. Both levels of control are assayed in 5 replicates, and the Mean and %CV are calculated. This mean serves as the Grand Mean for the Control Assigned Value Range Validation. The range is established as +/- 20% of the grand mean. The validation acceptance criteria is +/- 10% of the grand mean. The end users are instructed to establish their own range.

Conclusion:

The Tosoh Bioscience, Inc. ST AIA-PACK ACTH is substantially equivalent to the Roche Diagnostics Elecsys ACTH Immunoassay (k)060585 for the in vitro diagnostic use only for the quantitative measurement of ACTH in human EDTA plasma, on Tosoh AIA System Analyzer. Since ACTH is controlled by factors affecting the hypothalamic, pituitary and adrenal glands, the determination of ACTH level is useful in clinical investigation for diseases of these glands.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

TOSOH BIOSCIENCE, INC
c/o Judith Ogden
6000 Shoreline Court
Suite 101
South San Francisco, CA 94080

DEC - 1 2011

Re: k111335
Trade Name: ST AIA-PACK ACTH,
ST AIA-PACK ACTH Calibrator Set,
AIA-PACK ACTH Control Set
Regulation Number: 21 CFR 862.1025
Regulation Name: Adrenocorticotropic hormone (ACTH) test system
Regulatory Class: Class II
Product Codes: CKG, JIT, JJX
Dated: November 15, 2011
Received: November 16, 2011

Dear Ms. Ogden:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance...

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k111335

Device Name: ST AIA-PACK ACTH

Indication For Use: ST AIA-PACK ACTH is designed for IN VITRO DIAGNOSTIC USE ONLY for the quantitative measurement of adrenocorticotropic hormone (ACTH) in human EDTA plasma. Measurements of ACTH are used in the differential diagnosis and treatment of certain disorders of the adrenal glands such as Cushing's syndrome, adrenocortical insufficiency, and the ectopic ACTH syndrome.

Device Name: ST AIA-PACK ACTH Calibrator Set

Indication For Use: ST AIA-PACK ACTH Calibrator Set is designed for IN VITRO DIAGNOSTIC USE ONLY for the calibration of the ST AIA-PACK ACTH assay on Tosoh AIA System Analyzers

Device Name: ST AIA-PACK ACTH Control Set

Indication For Use: ST AIA-PACK ACTH Control Set is designed for IN VITRO DIAGNOSTIC USE ONLY for performing quality control procedures with the ST AIA-PACK ACTH assay on Tosoh AIA System Analyzers

Prescription Use ___√___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____ (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

K111335